**Cryptococcal meningitis**

**Signs and symptoms for the disease it produces**.

45 yr old **HIV+** male not currently on antiretroviral therapy:

**Fever, severe headache, nausea**, vomiting

**Mental status changes** that were progressive over the **past 2 weeks**

PE:

Lethargic and disoriented

**Nuchal rigidity**

**Positive Kernig sign** (flexion of the neck when the knee is flexed)

Labs:

CD4 count= 42 cells/microliter

**The source of infectious organism**.

*Cryptococcus neoformans* variant *neoformans*. Isolated worldwide from soil, usually associated with **bird/pigeon droppings**.

A less common etiological agent, *C. neoformans* variant *gattii* has been isolated from eucalyptus trees in tropical and subtropical regions.

**The manner of exposure, route of infection, tissues that they reside and, where appropriate, transmission to others**.

Transmission= Inhalation of airborne fungus. Usually an opportunistic infection and is NOT transmitted person-person.

**The pathology and the manner by which the particular disease develops**.

Primary infection of lung in most exposed individuals in asymptomatic. Some patients may develop:

Pneumonitis with fever, chills, cough and shortness of breath

Result of granulomatous inflammation

***C. neoformans* causes a deep mycosis in AIDS patients with low CD4 counts (<100)**.

Spreads from the lungs (where infection may be asymptomatic) to the bloodstream

Hematogenous dissemination to the CNS and other organs can occur during primary infection or reactivation

Cross the BBB and accumulate in the perivascular areas of cortical gray matter and other areas of the CNS

No toxin produced

Without cell-mediated immunity= Encapsulated cryptococci multiply and accumulate within brain parenchyma with little necrosis or organ dysfunction, and results in macroscopically visible gelatinous pathology.

Inflammatory response is minimal

CNS symptoms include gradual onset with worsening headache and fever over weeks

More severe cases are associated with altered mental status

CT or MRI are rarely positive for mass lesions

NOTE: Skin involvement after dissemination may cause acneiform (nodular) or molluscum-like lesions, ulcers, or subcutaneous tumor-like masses. Can find fungus in the lesions.

**Methods of identification and placement into a particular biological subset**.

**India ink stain in CSF or cryptococcal (latex agglutination) antigen test in CSF and serum**

India ink: Reveals budding cells, surrounded by a refractile, sharply demarcated capsule, this is diagnostic

Latex agglutination: Cryptococcus polysaccharide antigen

Cultures of CSF and blood for bacteria, fungi, and mycobacteria (would also do Gram stain and acid fast stain to rule out bacterial cause)

For confirmatory diagnosis and if India ink and antigen test fail

Cryptococcus: Yeast-like fungus (**NOT dimorphic**), with an oval, budding yeast cell. A thick, gelatinous capsule frequently surrounds yeast cells.

Grows well on standard media (Sabouraud-dextrose) at 37C. Highly mucoid, creamy-white colonies.

For culture ID: Urease +, phenol oxidase +, and they oxidize certain sugars and KNO3

**Factors leading to enhanced resistance or susceptibility.**

T cell deficiency/defect. Immunocompromised individuals are at risk for development of meningitis.

**Other organisms in the differential diagnosis and how to discriminate among potential causative agents**.

Bacterial meningitis: *M. tuberculosis, S. pneumoniae, T. pallidum*. Has more acute and severe presentation than is described in this case. Tuberculosis is also an important consideration because it is much more common in AIDS patients than in other populations. Syphilis is always a consideration, especially in AIDS, although it often manifests more indolently.

Brain abscess: Will often have associated focal neurologic findings.

Fungal meningitis: *C. immitis, C. neoformans, H. capsulatum*. **In patients with AIDS, Cryptococcus neoformans is the most common cause of meningitis**. Other fungi are uncommon causes.

Viral meningitis: HSV. Viral causes should not last this long.

**Prevention, treatment and vaccine design (live vs. dead**).

Prevention: Use of HAART therapy in AIDS patients to improve immune system.

Treatment: **Amphotericin B** (D.O.C.) + **Flucytosine** (5-FC) are often recommended for combination therapy. Fluconazole has been approved for acute cases but usually is used for maintenance therapy. Treatment is life long because of frequent relapses. Therapy may be discontinued if sufficient immune response restoration occurs (HAART). Itraconazole is sometimes used but is less effective due to poor penetration into CSF.